

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
23 June 2005 (23.06.2005)

PCT

(10) International Publication Number
WO 2005/055980 A3

(51) International Patent Classification⁷: A61K 47/48

(21) International Application Number:
PCT/US2004/040660

(22) International Filing Date:
3 December 2004 (03.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/527,330 5 December 2003 (05.12.2003) US

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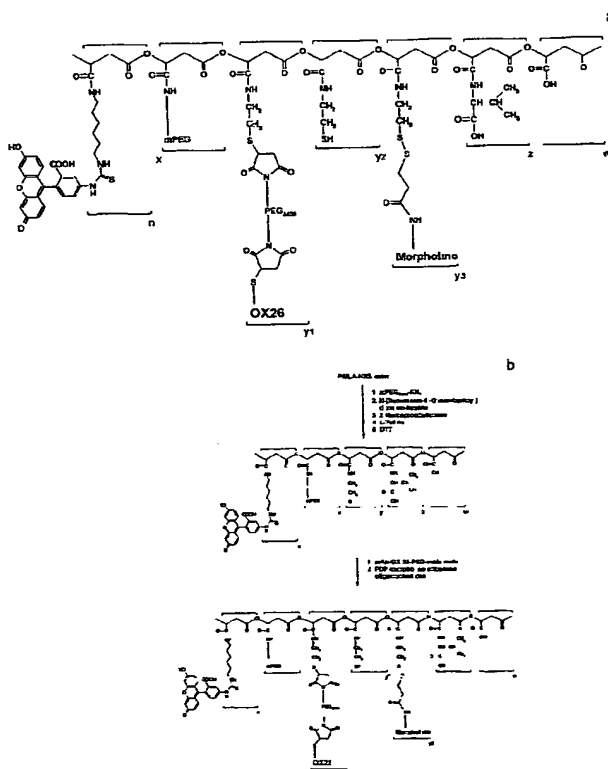
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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,

[Continued on next page]

(54) Title: POLYMALIC ACID-BASED MULTIFUNCTIONAL DRUG DELIVERY SYSTEM



(57) Abstract: A structured drug system that is useful for delivering a drug payload to a specific tissue or cell type is disclosed. The system is based on purified polymalic acid. This polymer isolated from natural sources is biocompatible, biodegradable and of very low toxicity. The polymer is extremely water soluble and contains a large number of free carboxyl groups which can be used to attach a number of different active molecules. In the examples disclosed N-hydroxysuccinimide esters of the carboxyl groups are used to attach such molecules. The active molecules include monoclonal antibodies to promote specific cellular uptake and specific pro-drugs such as antisense nucleic acids designed to modify the cellular metabolism of a target cell. The pro-drugs are advantageously linked by a somewhat labile bond so that they will be released under specific conditions. In addition, the system contains amide-linked valine to encourage membrane disruption under lysosomal conditions. Polyethylene glycol groups are attached to extend the drug system's circulation half-life. In addition, fluorescent reported groups can be readily included to aid in visualizing and confirming drug system targeting. The drug system can deliver treatments for a wide range of diseases and is specially advantageous for treatment of neoplasms.

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FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:

5 January 2006

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/040660

A CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K47/v48

According to International Patent Classification (IPC) or to both national classification and IPC

B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data, PAO

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>BULMUS V ET AL: "A new pH-responsive and glutathione-reactive, endosomal membrane-disruptive polymeric carrier for intracellular delivery of biomolecular drugs"</p> <p>JOURNAL OF CONTROLLED RELEASE, ELSEVIER, AMSTERDAM, NL, vol. 93, no. 2, December 2003 (2003-12), pages 105-120, XP004473631</p> <p>ISSN: 0168-3659</p> <p>page 111, column 2, paragraph 4; figure 1</p> <p>page 108, column 2, paragraph 3 - page 109, column 2</p> <p style="text-align: center;">-/-</p>	<p>1, 2, 6, 14, 18-20, 24, 25</p>

☒ Further documents are listed in the continuation of box C

☒ Patent family members are listed in annex

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Date of the actual completion of the international search

20 October 2005

Date of mailing of the international search report

02/11/2005

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/040660

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Inter ¹ ₂ Application No
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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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information on patent family members

International Application No

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